[00010] As used herein, the term "drug" is to be construed in its broadest sense to mean any material which is intended to produce some biological, beneficial, therapeutic, or other intended effect, such as permeation enhancement, for example, on the organism to which it is applied.

[00011] As used herein, the term "individual" intends a living mammal and includes, without limitation, humans and other primates, livestock and sports animals such as cattle, pigs and horses, and pets such as cats and dogs.

[00012] As used herein, the term "membrane functionality" refers to properties of the membrane which affect the desired degree of rate control of the drug delivery device in which the membrane is used and includes for example, drug permeability, water permeability, and/or water uptake.

[00013] As used herein, the term "transdermal" intends both percutaneous and transmucosal administration, i.e., passage of drug through skin or mucosal tissue into the systemic circulation.

SUMMARY OF THE INVENTION

[00014] According to this invention, rate controlling membranes intended for use in controlled drug delivery devices are pretreated by an annealing process prior to or subsequent to incorporation of the membrane into the drug delivery device. The annealing process of this invention provides rate controlling membranes which exhibit consistent membrane functionality over time. In one embodiment, the annealed rate controlling membranes of this invention comprise enhanced permeability compared to non-annealed membranes that is more predictable with respect to thermal transients, particularly throughout storage over time. According to another embodiment, rate controlling membranes subjected to the annealing process of this invention maintain a permeability within a preferred range even after being subjected to elevated temperatures.

[00015] Accordingly, it is an aspect of this invention to provide rate controlling membranes for use in controlled drug delivery devices that overcome the disadvantages associated with those of the prior art.

[00016] Another aspect of the invention is to provide rate controlling membranes which exhibit consistent membrane functionality over time.

[00017] Another aspect of this invention is to provide rate controlling membranes for transdermal drug delivery systems that have more predictable drug permeabilities with respect to thermal transients.

[00018] Another aspect of this invention is to provide rate controlling membranes for transdermal drug delivery devices that have drug permeabilities that are stable as a function of storage time.

[00019] Another aspect of this invention to provide rate controlling membranes for transdermal drug delivery devices that provide enhanced drug permeability.

[00020] Yet another aspect of this invention is to provide rate controlling membranes for fluid-imbibing drug delivery devices which exhibit consistent water permeability and water uptake over a storage period.

[00021] Therefore, the invention comprises the following aspects, either alone or in combination:

[00022] A rate controlling membrane for a controlled drug delivery device characterized by being subjected to an elevated temperate of about 30° C to about 5° C below the melting temperature of the membrane polymer for a predetermined period of about 1 - 250 hours and subsequently incorporated into the delivery device.

[00023] The membrane material may be selected from the group consisting of ethylene vinyl acetate copolymers, polyethylene, copolymers of ethylene, polyolefins including ethylene oxide copolymers such as Engage® (DuPont Dow Elastomers), polyamides, cellulosic materials, polyurethanes, polyether blocked amides copolymers such as PEBAX® (Elf Atochem North America, Inc.), and polyvinyl acetate.

[00024] The device may be a transdermal drug delivery device comprising a drug reservoir layer between a backing layer and a contact adhesive layer, wherein rate controlling membrane is on the skin-proximal side of the drug reservoir layer. The drug reservoir may also contain one or more permeation enhancers and/or other excipients.

[00025] The device may be a transdermal drug delivery device comprising a backing layer, a permeation enhancer reservoir containing a permeation enhancer on the skin proximal side of the backing layer, a drug reservoir layer containing at least one drug to be transdermally administered on the skin proximal side of the permeation enhancer reservoir, and a means for maintaining said drug device in drug transmitting relation with the skin, wherein the rate controlling membrane is positioned between the permeation enhancer reservoir and the drug reservoir.

[00026] Alternatively, the membrane may be positioned in sealing relationship with an internal surface of one end of an impermeable reservoir of a fluid-imbibing drug delivery device, wherein the fluid imbibing drug delivery device comprises an impermeable reservoir containing a piston that divides the reservoir into a drug containing chamber and a water-swellable agent containing chamber, wherein the water-swellable agent containing chamber is provided with an outlet which accommodates the membrane. The agent containg layer may comprise leuprolide.

[00027] The membrane may be cooled to ambient conditions before being incorporated into the delivery device.

[00028] Additionally, the invention is directed to a method for processing rate controlling membranes used in controlled drug delivery devices comprising:

a) exposing the membrane to a predetermined temperature of from about 30° C to about 5°C below the melting temperature of the membrane polymer;